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Editorial Comment

Program Highlights Some of the sessions which are of especial interest to the members of the American College of Chest Physicians, as taken from the program of the College meeting to be held at Atlantic City, June 6-8, are: "A Joint Session of the American Broncho-Esophagological Association and the American College of Chest Physicians"; "A Discussion of the Tuberculosis Problem from the Viewpoint of the Army, Navy, Veterans Administration, Public Health, and Organized Medicine"; "A Luncheon Meeting sponsored by the Council on Undergraduate Teaching in the Medical School"; and the "General Scientific Assemblies."

The Joint Session of the American Broncho-Esophagological Association and the American College of Chest Physicians will bring together the bronchologist, the chest surgeon and the internist in an interesting discussion concerning all phases of bronchoscopy.

The discussion of the tuberculosis problem from the viewpoint of the Army, Navy, Veterans Administration, Public Health and Organized Medicine, will be presented to us by Brigadier General Charles C. Hillman for the Army; Commander Robert E. Duncan for the Navy; Dr. Roy S. Wolford for the Veterans Administration; Dr. H. E. Hilleboe for the U. S. Public Health Service, and Dr. Esmond R. Long for the Committee on Tuberculosis of the National Research Council.

The meeting sponsored by the Council on Undergraduate Teaching in the Medical Schools will present the latest developments in the efforts of the College to interest the deans and faculties of our leading medical schools in the advancement of the teaching of tuberculosis and other diseases of the chest to our medical students. Dr. E. W. Hayes, Chairman of the Council, will bring us a report on the meeting of the Association of American Medical Colleges, which he attended as a guest speaker at Richmond, Virginia, last year. Other teachers who will speak at this session will be Dr. Jay Arthur Myers, Dr. A. J. Cohen and Dr. Ralph C. Matson.

C. M. H.

Goodwill Ambassadors This year, the medical meetings to be held at Atlantic City will give prominence to speakers and scientific exhibits from our good neighbors "South of the Rio Grande." We are more than pleased to welcome these grand fellows from our sister republics, who, by their presence, will express to us their deep feeling of comradeship in this great emergency.

The excellent scientific exhibits brought here from the Latin-American countries will be shown in the Scientific Assembly Auditorium at the American Medical Association meeting to be held at Atlantic City, June 8-12. We are happy to announce that some of these exhibits will be shown by Fellows of the American College of Chest Physicians from the Argentine. We are also happy to announce that places on our program will this year be occupied by Fellows of the College from Cuba, Mexico and the Argentine.

These men will travel long distances and endure many inconveniences in order to attend our meetings. It is up to us to show our appreciation to these goodwill ambassadors by making certain that there will be a good attendance at each of the sessions. Our guests will bring to us much beneficial information. We will also have an opportunity to meet and know our neighbors better. Every Fellow and Associate of the American College of Chest Physicians owes it to himself, his country, and his College to greet these Fellows at Atlantic City. The dates of the College meeting are June 6-8. F. W. B.

Chemotherapy of Tuberculosis and the Mode of Action of the Sulfonamide Compounds*

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There have been a significant number of papers dealing with the effect of various sulfonamide compounds on the tubercle bacillus. It is not important to refer to more than a few of these because, with the exception of the recent work of Feldman and his associates,[1] their therapeutic effect in experimental animals has not been of a critical nature.

Considered as a whole, the studies preceding Feldman's fall into two groups: first, those claiming a definite degree of protection; and second, those that failed to demonstrate such an effect. Among the latter group of investigators are Steinbach and his coworkers,[2] Kolmer and associates,[3] and Smithburn.[4] In the former category are Rich and Follis,[5] Locke, et al,[6] and Greey, Campbell and Culley.[7] The discrepancies appear to be accounted for largely by such variables as the size and duration of drug dosage, the intervals between doses, route of administration, etc. The species of animal used for test also plays some part.

The trials were not limited to sulfanilamide. Sulfapyridine, as well as a dodecanoyl derivative of sulfanilamide,[8] and certain acyl derivatives,[9] have also been employed. The most that has been accomplished with these compounds is the demonstration of a growth inhibition on the microorganism in vivo, but only as long as administration of the drug was continued. When it was withdrawn, the bacteriostatic effect disappeared.

However, the recent results obtained by Feldman[1] fall into a different category. They employed one of the better known sulfones against a variant of the classical H-37 strain of tubercle bacillus. The trade name of the drug is Promin. Chemically, it is the sodium salt of p,p'-diamino-diphenyl-sulfone-N,N'-dextrose sulfonate. Apparently it is inactive in this form, but when given orally, the sodium dextrose sulfonate is split off and the original diamino-diphenyl-sulfone is regenerated. This is its active form.

In one series of guinea pigs, administration of the drug was delayed as long as six weeks after inoculation of the organism and a positive tuberculin test was in evidence. The recovery of 7 out of 8 animals of this series proves beyond question that an active progressive tuberculosis was being treated. Indeed, about as large a percentage of animals recovered after a six weeks' interval between inoculation of the organism and administration of the drug, as occurred when both were given on the same day. Moreover, there was an inability of emulsions of their organs to infect fresh pigs on injection.

What may eventuate as an important conditioning feature of the experiments was the modest virulence of the tubercle strain employed. The RV (rough colony, virulent) H-37 strain employed by them is not of the high virulence of the S (smooth colony) phase and this is borne out by the 6-month period required for death of the untreated animals. A conditioning feature of another kind is the rather high toxicity of the drug, which becomes especially important in a chronic disease. Nevertheless, the experiments are sufficiently conclusive to justify therapeutic trials in man which, I understand, are now in progress. The authors are justifiably cautious in the clinical inferences drawn from their experimental work.

The Mode of Action of the Sulfonamide Compounds

We shall center our attention primarily on the drug's impact against the germ itself, inasmuch as the participation of the host's immunity mechanisms, although important, are at best secondary. Of the various hypotheses originally proposed, the ones being sustained by experiment are those connected with sulfanilamide's interference with the respiratory function of the microorganism —in other words, with its enzyme systems.

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* Read before the Seventh Annual Meeting of the American College of Chest Physicians, the Hotel Statler, Cleveland, Ohio, June 1, 1941.

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The first definite demonstration that an enzyme *per se* might be involved came from the studies of Locke and his co-workers[9] at the Institute of Pathology of the Western Pennsylvania Hospital. At about the same time Lockwood[10] suggested that a protease might be affected, by reason of peptone's interference with the action of sulfanilamide. In its original form, the theory pre-supposed that the free amino group of sulfanilamide had been oxidized to a moderate degree, because such oxidation products have been known previously to have very definite anti-enzymatic properties.

One of the products to which we refer is represented by Fig. 2 in the above diagram. Chemically it is a hydroxyl-amine derivative of sulfanilamide (Fig. 1). It has been demonstrated that this derivative completely inactivates the enzyme *catalase* and to a certain extent the enzyme *peroxidase*. This would mean that the hydrogen peroxide, a respiratory product that is normally produced by most strains of pneumococci and hemolytic streptococci would not be destroyed, and as a result, the microorganisms would be subjected to the rather considerable toxic action of this substance.

In support of the theory that this might constitute one of the mechanisms involved in the bacteriostatic action of the sulfonamide compounds are certain interesting clinical and experimental considerations. Thus, it has been shown by Shinn for the pneumococcus[11] that the bacteriostatic action of sulfanilamide on a susceptible strain is reduced in proportion as the aerobic conditions are diminished; and correspondingly, peroxide production falls off until under anaerobic conditions none is to be detected.

On the clinical side it is a well-known fact that abscesses and other necrotic foci are notoriously lacking in their oxygen content. Not only is the circulation of such foci seriously impaired, but the broken down products of pus such as the peptone-like substances tend to absorb any oxygen that might otherwise have entry into the focus of the infection. In other words, the local conditions are probably so largely anaerobic as to block effectively any oxidative changes in the sulfanilamide molecule. On the other hand, this evidence in behalf of the oxidative theory is scarcely more than presumptive, because there are other substances in pus which may have an important role to play. Moreover,

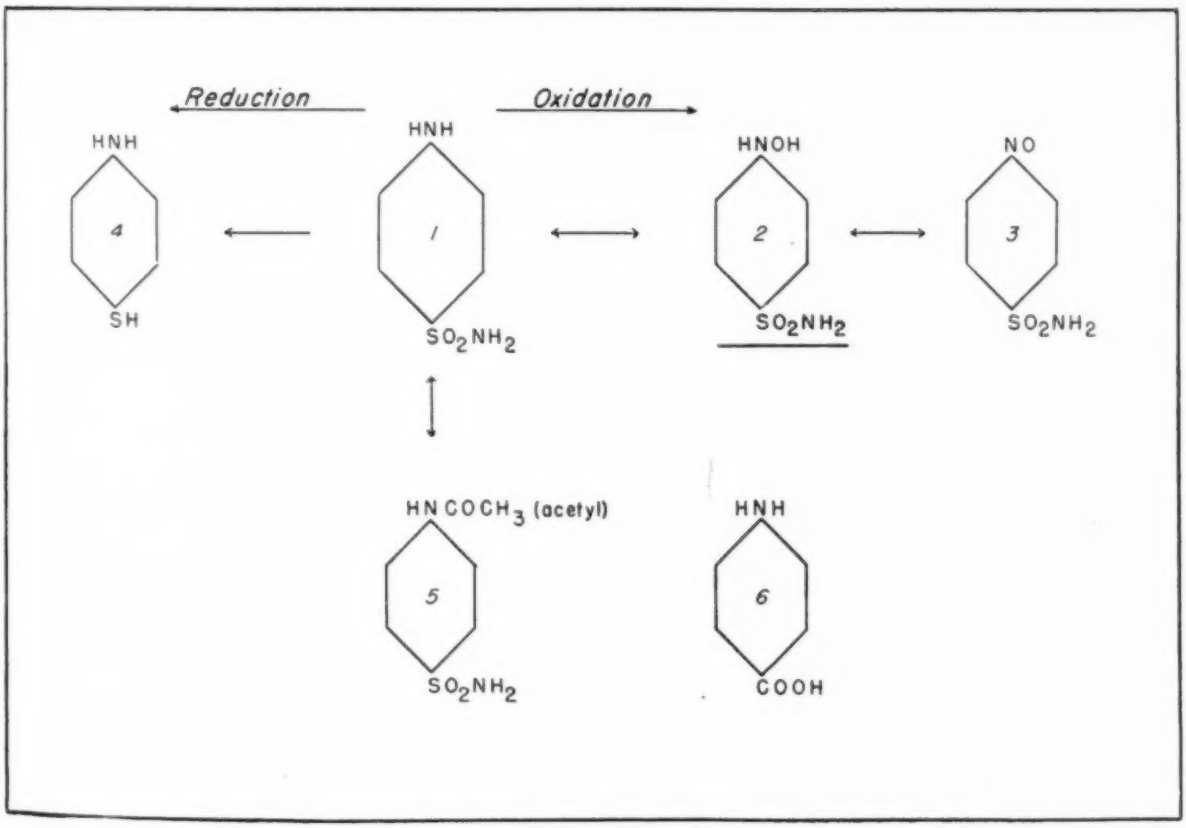

CHART I

it is by no means invariable that bacteriostasis may not take place under strictly anaerobic conditions, as indeed has been indicated in the Shinn experiments just quoted.

The latter point was brought to the fore particularly in the experiments of Broh-Kahn,[12] who showed that the colon bacillus under very stringent conditions of anaerobiosis is vulnerable to the bacteriostatic action of sulfanilamide. Moreover, under these conditions, sulfanilamide caused the poisoning of an oxygen transportase (enzyme), thus indicating that, for the inactivation of certain enzymes oxygenation of sulfanilamide's free amino group was not essential. As additional evidence for the enzyme inactivation theory are the studies of MacLeod,[13] who showed that certain dehydrogenases of the pneumococcus are also inhibited by sulfapyridine. These enzymes are also concerned with the germ's utilization of oxygen in its metabolism.

Furthermore, it is now clear that the clinical acidosis caused by sulfanilamide results from the inactivation of the enzyme carbonic anhydrase. This action is referable to the activity of the SO_2NH_2 group of the sulfanilamide molecule rather than to the free amino group (Fig. 2, Diagram I). The first indication of such an effect on this enzyme was the work of Locke which was referred to in our paper before the Ohio State Medical Society in May, 1940.[14] However, these experiments could not be completed until some months later.

Meanwhile, a paper by Mann and Keilin[15] appeared on the same subject and Locke's announcement came a few weeks later.[16] Thus, this observation was made independently by two different workers in different countries at virtually the same time; but if the ethics that have previously decided priority considerations continue to be practiced, not only will Mann and Keilin's work receive priority, but Locke's likely will be overlooked.

Despite the fact that there is considerable evidence in support of the oxidative enzymatic point of view, there is developing a gradual accumulation of experimental observations that, for the moment at least, are not to be reconciled with its oxidative aspects. For example, the inactivation of carbonic anhydrase takes place when the free amino group is inactivated by acetylation and is therefore not susceptible of oxidation (See Diagram I, Fig. 5). Furthermore, substituents of the SO_2NH_2 group such as thiazole or pyridine prevent the inhibition of carbonic anhydrase, even in the presence of an unblocked free amino group. Accordingly, it is the sulfonamide rather than the free amino group that is involved.

There is also the fact that Type 3, Group A, hemolytic streptococci have not yet been demonstrated to produce hydrogen peroxide and yet they are among the most vulnerable strains to the action of sulfanilamide. Again, the staphylococcus aureus produces catalase, but sulfanilamide is not critically effective against this organism. On the other hand, sulfathiazole is clinically effective and sulfapyridine somewhat less so. One can only infer that if catalase inhibition is involved at all, it is certainly not the only factor contributing to the bacteriostasis. Indeed this evidence is in line with our earlier assessment of the enzymatic theory, which was viewed as having a much broader coverage than its catalase-peroxide aspect.[17]

Nevertheless, it should not be lost sight of that, in localized infections where it is possible to combine the use of H_2O_2 and sulfanilamide, curative effects can be obtained in cases that have proved refractory to sulfanilamide alone or in combination with other antiseptic agents. This is strikingly illustrated by Schneider[18] in his report of two cases, one of osteo-periostitis and one of intramuscular abscess. The lesions were flushed out with the peroxide solution containing dissolved sulfanilamide.

In this connection Schneider quotes a pertinent experiment of Fox who found that the bacteriostasis resulting from the addition of small amounts of H_2O_2 to cultures of streptococcus hemolyticus containing 10 mgm. of sulfanilamide per 100 cc. of media, was more than 10 times greater than with corresponding amounts of sulfanilamide alone; and more than 200 times greater than the stasis produced by peroxide alone.

On the other hand, peroxide is capable of oxidizing other substances in wounds in addition to the sulfanilamide, although whether the net effect of such a reaction would help to overcome the infection is not clear. But the experiments of Burton and the McLeods[19] show that the bacteriostatic

effect of the oxidation products of sulfanilamide are much more effective against certain organisms than the unoxidized sulfanilamide.

An additional factor of importance appears to have been identified by Coburn and West.[20] It was already known from the studies of Knight[21] that in the presence of nicotinic acid, the staphylococcus aureus can synthesize co-zymase, a factor indispensable for its growth. However, the failure of this synthesis to occur in the presence of sulfapyridine has led Coburn and West to infer that the drug has blocked it. The chemical similarity of the pyridine nucleus with the nicotinic acid and adenine portions of the co-zymase molecule might well conduce to its interference with the synthesis of co-zymase, therefore explaining, at least in part, an increased specificity against this organism, over and above the action of sulfanilamide against it.

In this instance apparently, it is not a case of inactivation of the enzyme *per se*, but rather of blocking its action by interfering with its co-enzyme. It represents an application of a concept whose chemotherapeutic applications have been formulated by Fildes.[22] In his terminology the nicotinic acid is an "essential metabolite," because it forms the basis for the synthesis of co-zymase, to which he refers as a "growth factor."

Fildes and his associates had already worked out a similar situation for the hemolytic streptococcus and for the pneumococcus. In this case the essential metabolite proved to be p-aminobenzoic acid, whose chemical structure is shown in Diagram I, Fig. 6. It is seen to be strikingly similar to sulfanilamide, thus conducing to its chemical competition with the drug.* The fact that in the presence of p-aminobenzoic acid the bacteriostasis of sulfanilamide is dispelled is most significant and the evidence accumulating in behalf of this theory of the mode of sulfanilamide's action is indeed impressive. Although this reaction is demonstrated most readily in the test tube, it is also capable, apparently, of taking place in vivo. For example, mice which have been infected by streptococci, but given p-aminobenzoic acid at the same time, die in the presence of an otherwise curative dose of sulfanilamide.[24]

Locke,[9] who formulated the peroxide theory, is of the opinion that an important aspect of the competition between sulfanilamide and para-aminobenzoic acid consists in the greater affinity of the latter for O_2. In such event, it would deprive sulfanilamide of the oxidation considered necessary for its activation. Only experiments directed to this point could establish its validity. Again, it is conceivable that the two points of view supplement each other. That is to say, the entry of sulfathiazole into the co-zymase molecule might involve the oxidation of its free amino group. Here, again, experimental demonstration is required if the necessary reconciliation between the somewhat different mechanisms of enzyme inactivation is to be brought about.

The aspect of the enzyme-blocking point of view that appeals particularly to the author is the plausibility of the explanation that it offers for specificity differences. This has been partially accounted for above, in the increased action of sulfapyridine over sulfanilamide in staphylococcus aureus infections. A somewhat general similarity between the sulfapyridine and sulfathiazole molecules makes it probable that the same explanation also holds in the case of the latter. Indeed sulfathiazole is usually critically effective against staphylococci which cannot be said of sulfapyridine. This effect may in turn find explanation in the fact that sulfathiazole actually stimulates the respiration and possibly the local resistance of the tissues against this organism, as will be discussed presently.

If this rather brief review of what is known at the present time of the biochemical aspects of the mode of action of the sulfonamide compounds does nothing else, it should impress one with the complexity of the biochemical considerations involved. Indeed, it has been rather obvious from the beginning that no one simple explanation was destined to explain the mode of action of these drugs, particularly when it became clear that their respiratory mechanisms were probably primarily concerned. However, as time goes on, it becomes clearer that the growth inhibition, which is the keynote of the drugs' action, is to be thought of as a starvation

* On the other hand, Bliss and Long[23] in a recent paper show that structural similarity is not essential to competitive action; for methionine shows a marked antagonistic action toward sulfanilamide.

process. Thus the bacteria are denied essential food substances, either indirectly, as by the blocking of an enzyme, or directly by enzyme inactivation.

The Biological Responses of the Microorganism to Sulfanilamide

As far as the effect on the organism itself is concerned, the starvation process results in important changes in the virulent growth phase of the organism, whereby it is gradually deprived of this important property. Such deprivation finds expression in transformation of the organism to a succession of phases represented in the following diagram.

The mucoid organism represented by the circle to the left is the phase of highest virulence, but under the impact of the drugs' action there results a succession of phases which are identified in part by the morphologic alterations indicated in the diagram. The organism finally loses its capsule as indicated by the Neufeld negative reaction, at which time its virulence also disappears. Accompanying these morphologic changes is a progressive loss of its metabolic functions in reference first to its characteristic ability to produce methemoglobin, and second to ferment inulin, and third to produce hydrogen peroxide.

Significantly, too, as soon as these changes are initiated, the invasive characters of the bacteria are seriously interfered with and they become phagocytable, even while they are still encapsulated. The long chained forms, especially, have their metabolic balances so seriously disturbed that they often undergo autolysis.

These changes are reinforced considerably by the serum antibodies, as well as by the phagocytic ability of the host and the general forces of natural resistance that may be said to lie behind them. These latter Locke[25] has shown to be quite distinct from the antibodies *per se* and to be considerably under the influence of vitamins, particularly B_1 and C.

Factors of Natural Resistance in Chemotherapy

Quite distinct from the antibodies, the phagocytes, etc., are resistance forces whose nature is much less specific. Indeed, they are physiological or nutritional, being much influenced by certain vitamins and hormones.

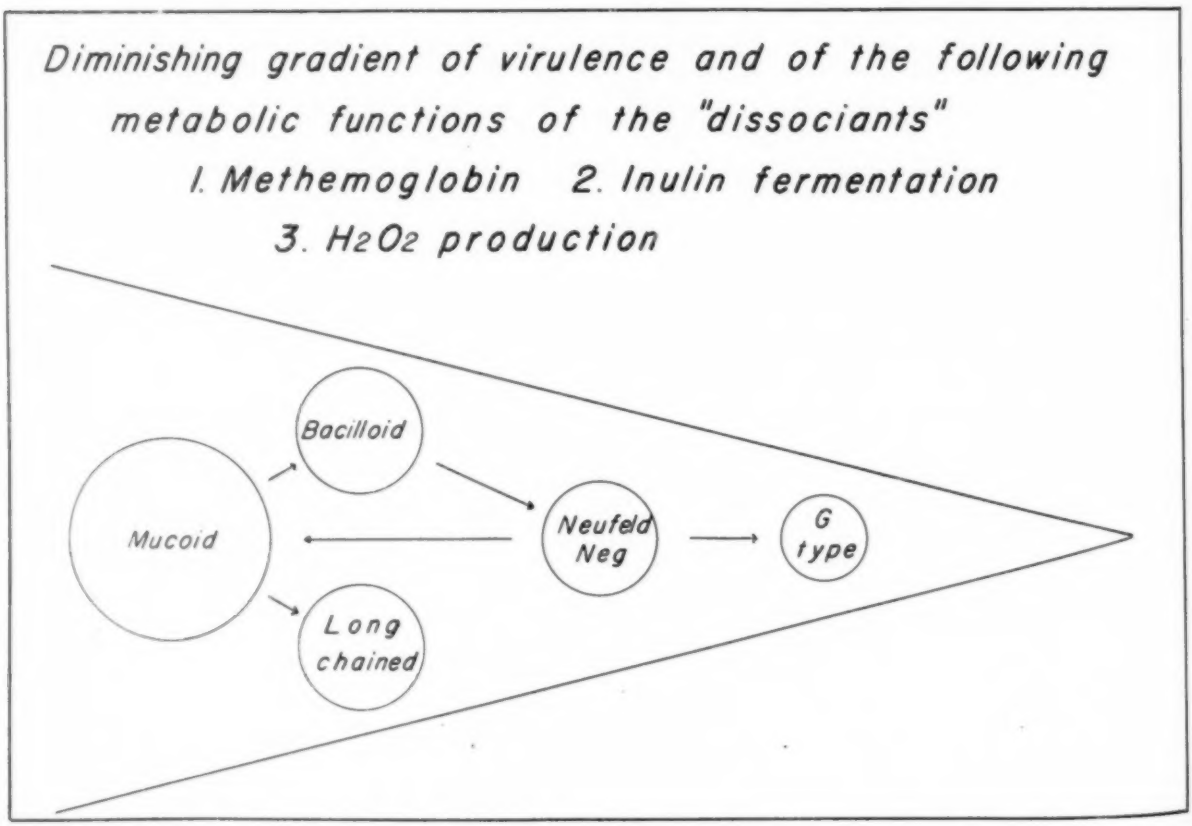

CHART II

Their effect in resistance against the pneumococcus is measurable by the rate at which the host can consume oxygen. However, there is an optimum range as can be demonstrated in the rabbit, for example.

Thus highly virulent pneumococci injected into a rabbit in the optimum range, are quickly removed from the circulation, whereas an animal varying much from this optimum in either direction will usually die of sepsis. Certain hormones, cortin particularly, and such vitamins as B_1, can reinforce this general resistance state very effectively as has been shown by Locke.

This fact gave us the idea originally of joining chemically vitamin B_1 to sulfanilamide, but this not being feasible, its thiazole nucleus was combined for us by Fosbinder and Walters [26] of the Maltbie Chemical Company of Newark, New Jersey. Whether the superiority of sulfathiazole over sulfanilamide against the pneumococcus, staphylococcus, etc., will find its entire explanation in its increase of tissue resistance (as measured by increased oxygen consumption, etc.) is doubtful, especially in view of the specificity trend shown in the experiments of West and Coburn.[20]

Nevertheless, experiments at present being conducted by us indicate that for certain tissues (Warburg technique) sulfathiazole produces a very appreciable increase in oxygen uptake, in contrast to sulfanilamide which in higher concentrations, depresses their normal rate of respiration, and in lower concentrations does not stimulate. There are numerous clinical instances coming to our attention where patients with low-grade infections have been cured with long-continued, but small, doses of the drug.

Finally, we wish to emphasize again that, in concentrating our attention in the beginning on the catalase-peroxydase system of enzymes, we had no intention whatever of attempting to limit the effect of the several sulfonamides' action to this one enzyme system. This, unfortunately, has been the unwarranted assumption of some writers.

Summary and Conclusions

In one of the sulfones is to be found the first chemotherapeutic agent against tuberculosis that has sufficient promise experimentally to justify a thorough-going trial clinically.

As regards the difficult problem concerning the mode of action of the sulfonamide compounds generally, it is becoming clearer that their biochemical effects are such as to interfere with the nutrition of the bacteria.

This they do by damaging their enzyme systems. Theoretically, this can come about in at least two ways; they may inactivate certain enzymes *per se*, or they may block enzyme action by interfering with the coenzymes.

Thus, the catalase-peroxydase system of enzymes can be inactivated by certain intermediate products of the oxidation of sulfanilamide. Hydroxylamine, or some related form, is perhaps the best example of this possibility.

On the other hand, sulfathiazole, presumably by virtue of the chemical constitution of its thiazole group, can interfere with the synthesis of co-zymase, a growth factor indispensable for the nutrition of the staphylococcus. Inasmuch as we are dealing with oxidation-reduction mechanisms, it is conceivable that these separate biochemical functions are complementary, at least in some instances. However, there is as yet no direct evidence on the point.

Anti-enzymatic action is likewise responsible for certain of the toxic effects of these drugs. Thus, the acidosis produced by sulfanilamide is referable to the inhibition of the enzyme, carbonic anhydrase, while the cyanosis is referable to a similar, if not identical, effect on hemoglobin. That is to say, it is partially oxidized to methemoglobin by the toxic NO_2 and NO derivatives of the free amino group of sulfanilamide.

Finally, certain of the sulfonamide compounds, such as sulfathiazole, seem capable of stimulating the rate of oxygen consumption of the body tissues, either as a whole or, in some instances, individual tissues. This all suggests that the effect of sulfathiazole on localized infections and on wound healing where no infection is involved, is due in part to an increase in tissue resistance.

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Tuberculous Tracheobronchitis*

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During the past two years approximately five hundred bronchoscopies have been performed on some two hundred patients in the University State Tuberculosis Hospital. Since July 1, 1940, bronchoscopy has been used as a routine diagnostic procedure without a single misadventure, for the vast majority of patients admitted to the hospital. It has been omitted or deferred only in a comparatively small group of patients in whom the procedure obviously would be of no diagnostic value or assistance, including those with no evidence of active pulmonary disease, very early cases with negative sputum and gastric wash, and very far-advanced, untreatable or terminal cases. The only contraindications which we have had occasion to respect were extreme illness, recent hemorrhage, and active laryngeal tuberculosis.

A few cases with retrogressive, quiescent, or inactive laryngeal tuberculosis have been bronchoscoped. These have included cases in which a persistent though inconstant positive sputum could not satisfactorily be accounted for on the basis of existing demonstrable lesions in the larynx or pulmonary parenchyma, a case that was bronchoscoped through a tracheotomy opening and a case which has twice been bronchoscoped for acute postoperative atelectasis. The laryngeal lesions have not been adversely affected in any of these cases.

The value and purposes of bronchoscopy in pulmonary tuberculosis are manifold. While recent hemorrhage is a contraindication which should not be disregarded, there is an occasional case in which determination of the source of hemoptysis is sufficiently important to outweigh the presumptive dangers of bronchoscopic examination. We have used bronchoscopy on two occasions for this purpose. In one case no information was forthcoming, in the other the blood was traced directly to the left upper lobe bronchus. In neither case was the severity of hemorrhage increased by the procedure.*

Bronchoscopy may also be useful when the

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* Recently a 15 year old girl was admitted as an emergency with profuse pulmonary hemorrhage. Portable radiograms revealed cavitation in the left upper lobe and atelectasis of the left lower. Bronchoscopy was considered indicated in an attempt to overcome the atelectasis and prevent further tuberculous extension by aspiration of blood clots and infected material from the bronchi.

source of a positive sputum is obscure. I am referring here to cases in which no specific lesions of the trachea or major bronchi exist. While one cannot strictly rely on specimens taken from individual bronchi through the bronchoscope, because of the danger of contamination, we have one case in which a right pneumothorax appeared completely effective and a previous lesion in the left lung had apparently disappeared, yet the sputum remained positive. Smears taken through the bronchoscope were negative on the right, but on the left revealed tubercle bacilli. Therefore, a left pneumothorax was induced and immediate sputum conversion resulted.

The symptoms of tuberculous tracheobronchitis are now well recognized. Their existence even in a case of pulmonary tuberculosis, however, is not necessarily diagnostic. We have one case in which bronchoscopy ruled out the presence of tracheobronchial lesions sufficient to cause the signs and symptoms observed. This case had a complicating "bronchial asthma." More frequently we see cases who have long been treated on an allergic basis when their asthmatic symptoms were caused by tuberculous lesions alone.

We have occasionally employed bronchoscopy in determining the presence, extent and location of bronchiectasis, both tuberculous and non-tuberculous. Selective iodized oil fillings of individual lobe bronchi may be accomplished very satisfactorily under bronchoscopic guidance. We have further employed bronchoscopy for drainage and insufflation of medications (e. g. sulfathiazole) in cases of bronchiectasis, and for aspiration of blocked secretions.

Bronchoscopies have been employed at the University State Tuberculosis Hospital primarily to determine the presence or absence of tuberculous tracheal and bronchial lesions and for the purpose of treating these when they exist.

The introduction of bronchoscopic examination as a part of the routine work-up in this hospital evolved from the feeling that an exact knowledge of the entire respiratory system, including the tracheobronchial tree, was important to a complete evaluation of the patient's condition and to the institution of the most appropriate treatment program. So far as I have been able to determine no one yet has recommended bronchoscopy as a routine procedure in active pulmonary disease. Many have considered active pulmonary tuberculosis a specific contraindication to bronchial endoscopy; others consider it indicated when, and *only* when definite signs and symptoms of tracheobronchial disease exist. McIndoe[1] and others reported on the use of routine bronchoscopy at the Michigan State Sanatorium between September, 1935, and April, 1937, and concluded that routine bronchoscopic examination is not necessary. It may be a long time before bronchoscopy is generally accepted as a routine diagnostic procedure in pulmonary disease. Possibly such a time will never occur. Our early experiences lead us to believe that it should and will.

Our reasons for the belief that routine bronchoscopy is of value will be covered in the report that follows. Among two hundred bronchoscoped patients who were admitted to the University State Tuberculosis Hospital with a diagnosis of pulmonary tuberculosis, there were fifteen in whom bronchoscopy helped to prove the absence of any significant tuberculous involvement; eight of these had a non-tuberculous bronchitis or peribronchitis, three had bronchogenic carcinoma, two had non-tuberculous bronchiectasis, one had metastatic pulmonary malignancy, one was later found to have Hodgkin's disease. There were also two cases in which bronchoscopic findings suggested that pressure from tuberculous tracheobronchial lymph nodes were responsible for the patients' symptoms.

Another case of bronchogenic carcinoma should also be mentioned here. This forty-six year old man was admitted with a positive sputum. While his x-ray was not typical of purely tuberculous involvement, it did reveal a small thin-walled cavity, and it is quite probable that discovery of the malignancy would have been delayed had he not immediately been bronchoscoped as a routine procedure. The bronchoscopic examination revealed a very small but suspicious mass in the dorsal branch of the right lower lobe bronchus. A biopsy diagnosis of epidermoid carcinoma of the bronchus was made. The discovery of an occasional operable case of bronchogenic carcinoma lends considerable weight to the argument for routine bronchoscopy.

So much has recently been written about

tuberculous tracheobronchitis,[2-15] its pathogenesis, its signs, its symptoms, that it would certainly be superfluous to repeat a formal or conventional discussion of this subject. The primary purpose of this paper is to present our findings, results and such conclusions as one may draw.

The pathogenesis of tuberculous tracheobronchitis has been ably discussed by many authors including Reichle and Frost,[16] Myerson[15], and Bugher, Littig and Culp.[4] According to Myerson,[15] the tracheobronchial lesions occur solely as a result of direct extension from the pulmonary focus by way of the bronchioles and bronchial submucosa. Since the lesions occur far more frequently in women than in men, who presumably are able to expectorate more efficiently; since the lesions usually occur on the posterior wall of the trachea and bronchi, where contact with infected secretions in the recumbent patient is likely to be more prolonged; and since we occasionally have seen isolated ulcers and tubercles, and these almost exclusively in women—we have come to believe that implantation or contact infection does occur.

There is an extraordinary variance in the incidence of tuberculous tracheobronchitis as reported by various authors. Bugher, Littig and Culp[4] found tracheobronchial lesions in 41 per cent of 122 autopsies. Flance and Wheeler[17] found evidence of gross involvement in only 3.1 per cent of 285 autopsied cases of pulmonary tuberculosis. McIndoe and his co-workers[1] found active or healed lesions in 11 per cent of 272 routine bronchoscopies. Hawkins[8] found gross bronchoscopic evidence in approximately 25 per cent of 516 selected patients at Olive View.

I have divided our cases into groups according to bronchoscopic findings. The first, or "bronchitis" group, consists of all cases in which the picture was primarily that of diffuse inflammation associated frequently with edema or infiltration of the mucous membranes. This rather heterogeneous group includes probably some cases whose membranes had become reddened merely as a result of cough or instrumentation. In others the inflammatory changes might be considered the result of a complicating non-specific bronchitis or a specific allergic reaction to the tuberculoprotein present in the sputum. Some of this group certainly represent the specific submucosal infiltrations which, according to Myerson,[15] are always precursors to the ulcerating or granulomatous lesions which may follow. The second, or ulcerogranuloma group, includes all those which presented active ulcerating or granulating lesions which might well be the source of tubercle bacilli in the sputum. The third group includes those in whom only fibrotic stenoses, presumably healed tuberculous lesions, were found.

In routine bronchoscopies of one hundred seventy tuberculous patients fifty-four, or 32 per cent, were classified in the first group; forty-nine, or 29 per cent, had ulcerogranulomas; and four, or 2 per cent, presented fibrotic lesions only. The remaining sixty-three (37 per cent) had normal findings in the visible portions of the tracheobronchial tree.

Our figures do not present a true picture of the incidence of tuberculous tracheobronchitis since a good many cases have been referred to us because this complication had already been diagnosed or suspected. It is also true that in a hospital dedicated primarily to the surgical treatment of tuberculosis the incidence of all tuberculous complications is likely to be high. However, realizing that many of the patients classified in our "bronchitis" group actually had tuberculous lesions in the bronchi, we are surprised to find the percentage of positive cases so much higher than in any other series reported, higher even than in those wherein patients have been selected for bronchoscopy only when suggestive signs or symptoms had previously been found.

There is no question that a clinical diagnosis of tuberculous tracheobronchitis can be made frequently and unmistakably. A persistent audible wheeze in the presence of active pulmonary tuberculosis is practically pathognomonic. The generally accepted diagnostic or suggestive symptoms and findings include the following:

1) Audible respiratory wheeze (this usually persists after all sputum has been raised. It is frequently very annoying to the patient who describes it as a rattling or gurgling. It may sometimes be heard across the room and is best elicited by auscultation in front of the open mouth of the patient).

2) Parasternal or substernal discomfort (the patient may complain of choking, pull-

ing or painful sensations and inability to take a deep breath. He usually can relate these sensations directly to the involved area).

3) Difficulty in raising sputum (the sputum is often extraordinarily viscid and tenacious).

4) Asthmatoid attacks or dyspnoea more marked than the pulmonary pathology would lead one to expect.

5) Capricious temperature elevations.

6) Cyanosis.

7) Parasternal rhonchi.

8) Signs of atelectasis or emphysema.

9) Marked variation in daily sputum volume or bacillus content.

10) Persistent or occasionally positive sputum in spite of well controlled parenchymal disease.

11) Bronchographic evidence of bronchiectasis, bronchial stenosis or ulceration.

12) X-ray evidence of "blocked" or "tension" cavities.

13) Atelectasis or emphysema as demonstrated by x-ray.

14) Hemoptysis, positive sputum or bronchogenic spread in the absence of pulmonary cavitation.

That the above criteria are not entirely reliable in the diagnosis of tuberculous lesions in at least the bronchoscopically visible portions of the tracheobronchial tree is suggested by the fact that nearly 40 per cent of our positive cases complained of no symptoms, and at least 10 per cent presented no suggestive physical or roentgenographic findings whatever. On the other hand, 25 per cent of the *negative* cases had symptoms, usually mild, and 50 per cent had one or more of the suggestive findings listed above. Reliance on the usual signs and symptoms of tuberculous tracheobronchitis will result in diagnostic errors in both directions.

That tuberculous tracheobronchitis has a definite deleterious influence on the course of pulmonary tuberculosis is corroborated by our findings which are summarized in the following chart:

	Stage of Disease			*Sex*	
	I	*II*	*III*	*M*	*F*
Negative	8%	24%	68%	51%	49%
Bronchitis	8%	22%	70%	39%	61%
Ulcero-granuloma	4%	35%	61%	31%	69%

Present Status of Known Cases	*Sputum* +	*Sputum* −	*Imp.*	*Unch.*	*Worse*	*Dead*
Negative	40%	51%	70%	19%	2%	9%
Bronchitis	58%	36%	68%	15%	11%	6%
Ulcero-granuloma	71%	16%	50%	30%	7%	13%

The prognosis of tuberculous tracheobronchitis has been considered extremely grave. Samson and co-workers[5] reported death in 52.9 per cent of ulcerative and stenotic cases, followed one or more years, or until death, with recovery in none. Jenks[10] stated that about 50 per cent die within one year of diagnosis. Our own experiences fail to corroborate such figures.

Since many of our patients have responded well to treatment we are in agreement with some of the more recent literature which indicates that the prognosis of tuberculous tracheobronchitis is not nearly as grave as the earlier reports suggest. It is, nevertheless, a very serious complication in that it may produce incapacitating symptoms in individuals who are otherwise in good general health. It may predispose the patient to serious and fatal complications such as empyema, bronchiectasis, atelectasis and bronchogenic spread. It may give rise to a small amount of positive sputum in patients who are clinically well. It is difficult or inadvisable to institutionalize such cases indefinitely since they are able and anxious to lead productive lives, and one hesitates to devote to them the hospital beds which are so much in demand. On the other hand, when at large, they constitute the true tuberculosis "carrier," a source of danger to others and also to themselves.

Various types of treatment have been recommended for tuberculous tracheobronchitis. They include: topical applications of silver nitrate (5-35 per cent),[8,10,11] electrocoagulation,[7,18,19] mercury vapor lamp,[20] x-ray[5,6] and radical surgery (pneumonectomy).[21,22]

We have had very satisfactory results in many cases with the use of silver nitrate (10-25 per cent). Electrocoagulation, we feel, is likely to produce excessive scarring with resultant stenosis. We have had no experience with irradiation therapy or pneumonectomy in these cases. We find that most isolated lesions will heal promptly following one

or more applications of 25 per cent silver nitrate. The greatest problem exists in the cases where considerable narrowing of the airway already exists at the time of diagnosis. It is our practice now to use 10 per cent silver nitrate for ulcero-granulomas producing, or bordering on, a stenosis, feeling that the more dilute solution is less likely to increase the fibrotic narrowing. Occasionally, when the active lesions have subsided, an attempt is made to dilate any remaining stenosis by the use of metal bougies. While mechanical dilatation and aspiration of retained secretions have undoubted value,[23] the results are usually temporary and the procedures may have to be repeated periodically.

Twenty-six cases of the ulcerogranuloma group received one to twenty-one topical treatments with 10-25 per cent silver nitrate. In four of these complete resolution of the lesions occurred. In fifteen there was apparently complete healing of the ulceration and granulation tissue, but more or less inflammation or fibro-stenosis remained. Six others showed improvement with or without stenosis, one remained unchanged, and none were worse. Of twenty-three cases who received no topical treatment, nine were bronchoscoped more than once over periods of one to twelve months. Of these, two showed complete healing, one was healed with residual stenosis, one was improved, two were unchanged, and three were worse.

Of nineteen untreated cases, four now have a negative sputum and three are dead. Of twenty-three treated cases, seven now have a negative sputum and two are dead—one of the latter having been in good general health with negative sputum for the four months immediately preceding her death. The present status of the seven remaining cases is not known.

In classifying and analyzing our findings some of the numbers become so small that they are of dubious statistical value. However, the general impression which we have gained, both through observation of our patients and review of our results, leads us to believe that topical treatment of the ulcerogranulomatous lesions is definitely worthwhile.

There is yet another aspect to the problem of tuberculous tracheobronchitis. The question has often been raised as to whether collapse therapy for pulmonary tuberculosis is contraindicated in the presence of this complication.

Samson,[5] in 1937, wrote "Because of the obviously poor prognosis we do not now recommend any type of collapse therapy for patients with ulcerative tracheobronchial lesions unless subsequent bronchoscopic examinations demonstrate a tendency for the ulcers to heal without the formation of an important stenosis." Eloesser[21] has said that collapse may be considered in total stenosis of a mainstem bronchus if the patient is afebrile and not toxic. In such a case collapse is particularly valuable in relieving complaints due to anatomical displacement. Jenks[10] believes that some form of permanent collapse (thoracoplasty) is preferable to a collapse procedure which is intended to be temporary (pneumothorax). Alexander[24] recommends the use of thoracoplasty in these cases only when bronchoscopic observation over a period of 3 months indicates that the tracheobronchial lesions are not progressive. It certainly is true that complete and permanent atelectasis is more likely to occur when pneumothorax is used in these cases, with the result that the pneumothorax must be maintained indefinitely and an excessive reduction of vital capacity results. Our experiences also indicate that tuberculous empyema more frequently complicates a pneumothorax when tuberculous bronchial lesions are present. I have insufficient evidence to substantiate the possible cause and effect relationship. The hazard of tuberculous empyema, if its likelihood can be proven, is certainly serious enough to contraindicate the use of artificial pneumothorax in these cases. While almost all of our cases who have had sputum conversion were treated by pneumothorax or oleothorax, associated with bronchoscopic applications, the majority had had pneumothorax induced prior to the discovery of the tracheobronchial complication. In practically every instance one can foresee that re-expansion of the lung will prove impossible. On the other hand, we do not yet have any evidence that other forms of collapse therapy may prove more consistently successful in these cases. By reducing the tussive force and permitting bacillus-laden sputum to remain longer in contact with the mucous membranes, it is possible that collapse therapy en-

hances the production and propagation of bronchial and tracheal lesions. This cannot be considered a contraindication to collapse of large parenchymal cavities and progressive pulmonary disease. It may well cause us to postpone collapse of non-excavating lesions. A number of our most serious cases had no evidence of cavitation when collapse therapy was instituted.

In conclusion, I would like to emphasize the value of bronchoscopic examination in pulmonary tuberculosis. It is our impression that it has proven itself of inestimable value both in diagnosis and in treatment. Serious and fatal complications of bronchoscopy in tuberculous patients have been reported. Samson[5] reports three cases in whom tracheotomy was necessary for post-bronchoscopic laryngeal edema. All of them died. In a pathological conference at Sea View Hospital[25] is reported a case where instrumentation resulted in freeing of bacillus-laden caseous material which was aspirated into the "good" lung and followed by rapid bronchogenic spread and death. We feel that in proficient hands, with a well-trained, cautious operating force, the dangers of bronchoscopy in tuberculosis are minimal. More than five hundred bronchoscopies have now been performed at the University State Tuberculosis Hospital on patients from two to seventy-one years of age. In not one single instance has the procedure been harmful in any way to the patient's welfare.

It is my fervent hope that routine bronchoscopies in this and in other institutions will lead us to a better understanding of tuberculous tracheobronchitis. Through periodic examination of cases of pulmonary tuberculosis a knowledge of the pathogenesis, evolution and response to treatment of this condition will be gained. And, eventually we may expect to discover the most effective methods for managing cases of pulmonary tuberculosis in which this distressing complication exists.

Summary

From experiences with five hundred bronchoscopies at the University State Tuberculosis Hospital the following conclusions have been drawn:

1) Pulmonary tuberculosis per se is rarely, if ever, a contraindication of bronchoscopy.

2) Bronchoscopic examinations afford valuable diagnostic information in pulmonary tuberculosis.

3) The incidence of specific tracheobronchial lesions in pulmonary tuberculosis is higher than generally recognized.

4) Tracheobronchial lesions are not of such grave prognostic significance as some authors have led us to believe.

5) Topical applications of silver nitrate solution in dilutions of 10 to 25 per cent appear useful in promoting resolution and healing of the tuberculous lesions found in the trachea and major bronchi.

6) The information to be gained from bronchoscopy, bronchography and cavity pressure studies will doubtless prove important in determining the most rational course of therapy for the individual tuberculous patient. Many failures not only may be anticipated but also may be avoided if, recognizing their indications, these procedures are judiciously employed.

7) The use of routine bronchoscopies in tuberculosis institutions is recommended in order that our understanding of tuberculous tracheobronchitis may be improved and in order that we may determine the most rational management of cases of pulmonary tuberculosis in which this complication exists.

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Spontaneous Hemopneumothorax
With Report of a Case

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Idiopathic spontaneous hemopneumothorax is a rather uncommon condition. A comparatively small number of cases is found reported in the literature. No doubt more cases have been found, but have not been reported either because there was hesitation in reporting a single case or because a busy chest service may find several cases after an earlier reported case, and would not report these. Some cases, in all probability, have gone unrecognized and have possibly been diagnosed as spontaneous pneumothorax with an effusion. Thoracentesis would have shown the correct diagnosis.

Pitt,[1] in 1900, is usually considered the first to report a case. He stated that there was no reference to this condition in any previous literature of this country or Europe. Hopkins[2] believes that Laennec[3] was the first to describe this condition, although the latter incorrectly assumed the presence of air in the pleural cavity to be due to a by-product of blood decomposition. In 1935, Frey[4] reported a case, and a review of the literature for the previous 34 years revealed only 13 cases. In 1937, Hopkins reviewed the literature and found 43 cases, to which he added three of his own cases, one being the first hemopneumothorax found in a woman. Since then, several additional cases have been reported in American and foreign literature.[5,6,7,8,9,10,11,12] Louria[13] presented five cases and one autopsy. Wiener and Jackson[14] had a case of thoracoplasty with spontaneous hemopneumothorax on the contralateral side. The hemopneumothorax occurred in about equal instances on the left and on the right side. Almost all the cases occurred between 20 and 40 years of age, and overwhelmingly in the male.

The cause of this condition is quite controversial. Kjaergaard[15] believed the condition was brought on when a ball-valve mechanism existed in a vesicle causing a gradual increase in pressure and eventual rupture. This would not seem to explain the massive hemorrhage usually found since the vesicle walls are thin and only very small vessels are found here. Hopkins presents the theory that the collapsing lung in the formation of a pneumothorax tears the pleural adhesions, containing blood vessels. This would explain the early hemorrhage and also why some have a late appearance of hemorrhage after pain. Large early hemorrhages occur when large vessels are torn. The late appearance of hemorrhage after pain is to be explained by assuming that the first pain is due to rupture of a bleb and the subsequent sharp pain is due to ripping of an adhesion containing blood vessels. Yet, the case reported by Jones and Gilbert[16] came to autopsy on

the 38th day, and the site of bleeding could not be found. Louria's case at autopsy also did not reveal the source of bleeding, although there was found a ruptured emphysematous bleb.

Cummer[17] felt this so-called idiopathic condition was the result of latent nondemonstrable tuberculosis. Weber[18] believed the condition resulted from a rupture of a minute superficial emphysematous bleb adherent to the parietal pleura, and itself resulting from a healed tubercle.

We see on thoracoscopy, in cases of spontaneous pneumothorax, a lung with superficial blebs, often in the upper lobe. Several of these blebs may or may not be attached to an adhesion from the parietal pleura. Certainly it would seem logical in cases of spontaneous hemopneumothorax to assume the bleeding to result from torn vessels lying in the adhesions.

Spontaneous hemopneumothorax has also been reported by Aguilar et al[19] in lymphatic leukemia, by de Barrin[20] in pulmonary metastasis of sarcoma, and by Raimondi et al,[21] Dufourt et al[22] and Beatty[23] in pulmonary tuberculosis.

The onset of this condition is usually quite dramatic. Sudden chest pain is the first symptom and the amount of the accompanying respiratory distress depends upon the rate the air enters the pleural space. Where the tear is comparatively large and a ball-valve mechanism is present, the displacement of thoracic organs is early and pronounced. The pain is local at first and then becomes diffuse, extending even to the abdomen. Hemorrhage may be prompt or delayed, and the degree of shock varies with the degree of hemorrhage. The pallor of the patient is marked and the skin is cold and clammy. In most instances, the patients had apparently been in good health, complaining possibly only of a slight cough. The condition manifested itself regardless of exertion, usually during mild activity.

So pronounced have been the symptoms in some cases that they were thought to have been caused by abdominal pathology. Milhorat's[24] case simulated appendicitis. So did the one of Jones and Gilbert. Fischer's[25] case was operated on for a ruptured duodenal ulcer but no abdominal pathology was discovered. A thoracentesis cleared the diagnosis. Frey's case was thought at first to be an acute gall bladder. Hurxthal[26] reported a case who presented a rigid, tender abdomen so that surgical intervention was considered.

Abdominal rigidity is probably due to basal pleurisy. Unless a careful physical examination is made, the diagnosis will be missed. The finding of a patient in shock, with a history of sudden pain over the left precordium may also make one think of a coronary occlusion. Sloer[27] presented such a case.

Physical examination reveals the immobile, ballooned hemithorax with hyper resonant percussion and absent breath sounds. Distant amphoric breathing may be heard, accompanied by whispered pectoriloquy. At the base, there is flatness because of the fluid. The speed with which this accumulates is much more rapid than in simple effusion. The uninvolved lung presents exaggerated breath sounds.

The insult to the pleura both by the rupture of the bleb and the escaping blood into the pleural space causes the formation of some pleural effusion. The effusion prevents the blood from clotting because it undoubtedly contains anticoagulants. It has long been known that blood in the pleural cavity does not clot. In my case, the aspirated blood did not clot or change viscosity standing in a beaker at room temperature for over three days. I sent the first specimen of clear pleural effusion from case of pulmonary tuberculosis to Dr. Harry Wallerstein, a hematologist, for experimentation. He reported back that the addition of the pleural fluid to fresh, uncitrated blood prevented it from clotting. This proved that pleural fluid contains anticoagulants and must be present in a hemopneumothorax.

Head[28] writes that when blood escapes into the pleural cavity, normal cardio-respiratory physiology is attacked from several angles. Progressive decrease in blood volume is complicated and aggravated by collapse of the lungs and by pressure upon the heart and great veins. Either of those conditions may cause death. Combined, they supplement each other. Hemorrhage produces: (1) progressive decrease in blood volume; (2) progressive decrease in cardiac output; (3) progressive fall in blood pressure; (4) shock from lack of oxygen supply to the vital nerve centers.

The two conditions supplement each other as follows: (1) Collapse of the lungs decreases oxygen saturation of blood, the volume of which has been decreased by hemorrhage, and so contributes to failure of oxygenation of the vital centers. (2) Pressure in the pleural cavity obstructs the return of venous blood to the heart. This hindrance is more effective and serious if the venous pressure is already lowered by a decrease in blood volume. (3) Both the obstruction to venous return and decreased blood volume diminish the cardiac output. (4) Exaggeration of the respiratory waves of blood pressure tends eventually to lower the mean blood pressure, and so augments a similar effect of decreased blood volume.

From these considerations it is obvious that an individual can tolerate a higher intrapleural pressure if his blood volume has not been decreased by hemorrhage and that he can stand a greater decrease in blood volume if his respiratory and circulatory systems are not compromised by a high pressure in the pleural cavity. The author therefore suggests the prompt use of blood transfusion, even using 1,000 cc. of blood taken from the pleural cavity, and injecting into a vein of a patient with a traumatic hemopneumothorax. There were no untoward complications.

Treatment depends upon the severity of symptoms in each individual case. The mild case needs nothing more than rest and mild sedation. The severe case requires immediate treatment. Rest, adequate sedation, oxygen and prompt blood transfusion are indicated. It is believed by some that since transfusions raise the blood pressure, they prolong the bleeding, and it would therefore be wiser not to give them. I certainly can see no reason why small transfusions should be withheld when these might be life saving. Some believe that the blood should be aspirated and replaced by air. Others are more conservative and leave the blood to act as a tampon. The blood is eventually absorbed, even though very slowly. It might be drawn off after the bleeding has apparently stopped for several days, and replaced by air. Decompression thoracentesis should be used very cautiously, and only when cardiac and respiratory distress is extreme. My case was treated conservatively and made an uneventful recovery. Two small late aspirations of bloody fluid were made in the hope of speeding up the lung reexpansion. Air should always be used to replace the aspirated fluid. Once the lung has reexpanded, pleural symphysis occurs. There is no record of a recurrence of spontaneous hemopneumothorax.

*Case Report**

J. G., age 24, male, white, single, clerk. Familial history negative. Always underweight. Height 71½ inches. Weight 118 lbs. First visit to family physician in September, 1938, for slight cough. Examination and fluoroscopy negative. Basal metabolism minus 16. Cough mild, but returned at irregular intervals until present pulmonary accident. On the evening of Nov. 24, 1939, after returning from a leisurely walk of several miles, was suddenly seized with pain in the left chest, became dyspneic and fainted. Recovery was fairly prompt but dyspnea returned severely the following morning. His family physician then visited him and found a left pneumothorax with fluid. A portable x-ray revealed a complete left pneumothorax with fluid up to the 4th rib. Mediastinum and contents were displaced to the right. I was called to see the patient on the evening of Nov. 25, 1939. Physical examination revealed a pale, thin individual presenting moderate dyspnea. His left hemithorax was ballooned and immobile. Percussion note was hyper resonant in the upper half and flat in the lower half. Breath sounds were absent. There was faint whispered pectoriloquy heard above the fluid level. Trachea and heart were found displaced to the right. On the right, percussion note was resonant and the breath sounds exaggerated and harsh. A diagnostic tap produced blood. The patient was treated symptomatically and made an uneventful recovery. One hundred and fifty cc. of dark blood was aspirated one month and two months later and replaced by air. This blood also did not clot after standing in a beaker for three days. Blood count on Dec. 2, 1939, showed 60 per cent (Dare) hemoglobin, R. B. C. 3,300,000, W. B. C. 13,650. Differential was normal. Achromia and anisocytosis were present. Poikilocytosis was very slight. No nucleated cells were present. The

* I am indebted to Dr. Benjamin Feldstein, of New York City, the patient's physician, for his kind cooperation in presenting this case.

blood picture later returned to normal. Animal inoculation of pleural blood and concentrated sputa examinations revealed no tubercle bacilli. Wasserman was negative. Temperature went up to 100° and lasted only 2 to 3 days. X-ray on Feb. 26, 1941, revealed a completely re-expanded lung with thickened pleura at the extreme apex and base. No pulmonary pathology was visible. To date the patient has been symptom free. He has gained over 30 pounds and is working regularly in his normal occupation.

Summary

1) Idiopathic Spontaneous Hemopneumothorax is uncommon.

2) The etiology is still controversial.

3) Symptoms may appear insidiously or severely.

4) The effect of physical exertion is questionable.

5) Onset may suggest abdominal or coronary pathology.

6) Concomitant pleural effusion is present.

7) Anticoagulants are present in the effusion.

8) Treatment consists of rest, adequate sedation, oxygen, blood transfusion, and aspiration of blood with replacement by air.

1750 Grand Concourse.

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Additional Report

Since presenting the above case, I have had the opportunity of seeing another case of spontaneous hemopneumothorax. H. S., slender white male, aged 39. This patient was under the care of Dr. George Bellos, of New York City, for a severe neglected case of diabetes. With the aid of large doses

of insulin, the patient's condition finally improved. Soon afterwards, he again began to lose weight and his physician found an early pneumonic process in the left hilus. There were no symptoms referable to pulmonary pathology. Sputum was negative but smears of gastric contents were full of tubercle bacilli.

I saw the patient first on Oct. 31, 1941, and instituted pneumothorax on the left side in an attempt to control the pathology. The lung collapsed easily and no adhesions were apparent. Subsequently, a considerable pneumothorax space was obtained. About three and a half weeks after the initial pneumothorax, and four days after his last refill, the patient found himself becoming moderately dyspneic. Temperature soon ranged between 101 and 102½ degrees. Fluoroscopy revealed an increase of approximately two interspaces in the small amount of fluid already present. A diagnostic tap produced hemorrhagic fluid which did not clot. The hemopneumothorax in this case was not due to external trauma but was on a tuberculous basis. Since the general condition of the patient was fair, treatment consisted of bed rest, sedation, and fluid aspiration with replacement by air.

The Problem of Pulmonary Tuberculosis in the Navy

LIEUTENANT COMMANDER E. RICEN
Medical Corps, United States Navy
Washington, D. C.

The problem of pulmonary tuberculosis in the Navy today consists of far more than merely diagnosing and treating this disease in Naval personnel. Certain environmental conditions exist aboard ship which are peculiar to the Navy alone and which play a part in contributing toward the incidence of pulmonary tuberculosis in naval personnel. Medical officers are constantly studying with a view to discovering methods of eliminating these hazards. The ultimate disposition of all cases of pulmonary tuberculosis requiring further treatment and follow up is another matter for consideration. Close cooperation exists between the Navy, American Red Cross, local health departments and the Veterans Administration in the disposition, treatment and follow-up of all naval personnel discharged from the service with pulmonary tuberculosis. The problem of dependents of naval personnel who have contracted this disease is still another one which the Navy handles through its outpatient department. Chest films, sputum examinations, and other laboratory tests on dependents are part of this service. Report of these cases to local health departments, follow-up and treatment are all included in this service. Another important ramification of the problem of pulmonary tuberculosis lies in the study and application of those methods which will result as far as possible in the elimination of endemic pulmonary tuberculosis. Accurate statistical data must be kept and studied from year to year in order to analyze the results achieved from changes in methods and policies.

The various ramifications of the problem of pulmonary tuberculosis in the Navy have been briefly indicated in order to emphasize the extent of this problem. A more detailed discussion of its various phases follows below.

The arduous nature of duty in the naval service under peace time conditions as compared to the work the individual may have been engaged in prior to his enlistment oftentimes may tax his resistance to the utmost. Naval duty afloat subjects a man to call twenty-four hours a day. As emergencies arise he may be called upon to put forth a maximum effort, for an extended period of time, under the most difficult working conditions. Once again before he has had sufficient rest, situations may arise which necessitate his presence at his battle station. Irregular habits of eating and sleeping are inevitable under such strenuous activity. Even

at best, compared to civilian standards, living conditions are somewhat crowded. In ships of the destroyer type and smaller, the same compartments are often used for eating, sleeping and recreation. Such environmental conditions predispose toward the development and spread of diseases of the respiratory tract. It makes the early detection of acute diseases of the respiratory tract and pulmonary tuberculosis imperative. A single case of active pulmonary tuberculosis expectorating positive sputum under such circumstances would, if undetected, probably result in further cases. Facilities for recreation and relaxation are too often limited in frequency and extent. The problem of maintaining physiological resistance under ordinary working conditions is therefore a far more difficult one among naval personnel. Lack of adequate physical and mental rest thus intensifies the problem of maintaining physiological resistance aboard ship. Various physical factors also play a part in diminishing the individual's resistance, some of which may have both a direct and indirect part in laying the ground work which precedes the development of pulmonary tuberculosis. Extremes of temperature and climate are commonplace in naval duty. This may vary from Arctic areas with prolonged periods of exposure to the elements and subzero temperatures, to duty in tropical zones. The incidence of tuberculosis in the white race is greater and the spread much more rapid in tropical and sub-tropical climates. Here again the early detection and isolation of all such cases is of great importance. Naval personnel may be exposed to altitudes of 30,000 feet above sea level in connection with flight duty; other duty may include descents to 400 feet below sea level while working with diving units. Arduous though these various types of duty may be, such conditions are all accentuated under war time conditions. The summation of all these factors plays a role in the diminished individual resistance to Mycobacterium Tuberculosis Hominis.

The mission of the Medical Corps of the Navy is to keep as many men at as many guns as many days as possible. The number of sick days and loss to the service resulting from hospitalization due to pulmonary tuberculosis seriously interfere with this mission. Prior to detection and hospitalization numerous sick days and decreased efficiency of the ship's organization may result. This is especially applicable to men in key positions. It is a function of the Bureau of Medicine and Surgery to keep and analyze all statistical data pertaining to pulmonary tuberculosis as well as other diseases. The admission rate per 100,000 for all forms of tuberculosis is in all instances based on the average naval strength for the current calendar year. Statistics on tuberculosis for the years 1934-1938 are presented below. Tuberculosis is treated as a separate class in the United States Navy Nomenclature of Diseases and Injuries.

The admission rate of all forms of tuberculosis was 163 per 100,000 as compared with 182 in 1933 and 176, the median rate for the preceding 5 years. There were 39,783 sick days reported for tuberculosis (all forms). The non-effective ratio per 100,000 or the

TUBERCULOSIS (All Forms) 1934

DISEASE	Admissions	Admission rate per 100,000	% of class Admissions	Sick days per case	% of class sick days
Tuberculosis, pulmonary, chronic, active	146	133.48	82.02	134.2	83.00
Tuberculosis, unclassified.	20	18.28	11.24	104.1	10.20
Tuberculosis, pulmonary, chronic, arrested	6	5.49	3.37	97.0	5.12
Tuberculosis, pulmonary, acute, pneumonic	4	3.66	2.25	87.4	1.54
Tuberculosis, pulmonary, acute general miliary	1	.91	.56	45.0	.11
Tuberculosis, general miliary.	1	.91	.56	9.0	.02
TOTAL FOR ENTIRE CLASS	178	162.73	100.00	126.3	100.00

daily average number of patients under treatment, was 100 as compared with 103, the median for the preceding 5 years.

The admission rate for all forms of tuberculosis was 131 per 100,000 as compared with 163 in 1934 and 170, the median rate for the preceding 5 years.

A total of 32,150 sick days was recorded for tuberculosis (all forms), or a daily average of 77 per 100,000 patients constantly on the sick list. The median non-effective ratio for the preceding 5 years was 100.

The admission rate for all forms of tuberculosis was 136 per 100,000 as compared with 131 in 1935 and 170, the preceding 5 year median. Tuberculosis (all forms) was responsible for 34,536 sick days, or a daily average of 76 per 100,000 patients constantly on the sick list. The median non-effective ratio for the preceding 5 years was 94.

The admission rate for all forms of tuberculosis was 114 per 100,000 as compared with 136 in 1936 and 170, the preceding 9 year median. A total of 37,894 sick days was recorded for tuberculosis (all forms), or a daily average of 78 per 100,000 patients on the sick list. The median non-effective ratio for the preceding 9 years is 95.

The admission rate for all forms of tuberculosis was 87 per 100,000 as compared with 114 in 1937 and 170, the preceding 9 years median. Tuberculosis (all forms) was responsible for 33,182 sick days, or a daily average of 65 per 100,000 patients on the sick list. The median non-effective ratio for the preceding 9 years is 94.

An analysis of these statistics will reveal that the admission rate for tuberculosis has dropped from 1.63 per 1,000 in 1934 to .87 per 1,000 in 1938. The non-effective ratio

$$\frac{\text{(number of sick days per year x 1,000)}}{\text{(average strength x 365 (or 366)}}$$

for this same period dropped from 1.00 per 1,000 in 1934 to .94 per 1,000 in 1938.

At this writing the last statistics include

TUBERCULOSIS (All Forms) 1935

DISEASE	*Admissions*	*Admission rate per 100,000*	*% of class Admissions*	*Sick days per case*	*% of class sick days*
Tuberculosis, pulmonary, chronic, active	121	105.97	80.67	131.8	88.58
Tuberculosis, unclassified.	16	14.01	10.67	61.4	5.92
Tuberculosis, pulmonary, chronic, arrested	6	5.25	4.00	70.4	3.50
Tuberculosis, pulmonary, acute, pneumonic	5	4.38	3.33	71.6	1.56
Tuberculosis, pulmonary, acute general miliary	2	1.75	1.33	50.0	.31
Tuberculosis, Skin	0	0	0	42.0	.13
TOTAL FOR ENTIRE CLASS	150	131.36	100.00	117.8	100.00

TUBERCULOSIS (All Forms) 1936

DISEASE	*Admissions*	*Admission rate per 100,000*	*% of class Admissions*	*Sick days per case*	*% of class sick days*
Tuberculosis, pulmonary, chronic, active	144	115.75	85.21	141.7	88.61
Tuberculosis, unclassified.	11	8.84	6.51	91.9	5.32
Tuberculosis, pulmonary, chronic, arrested	5	4.02	2.96	86.9	3.52
Tuberculosis, pulmonary, acute, pneumonic	4	3.22	2.37	80.0	1.62
Tuberculosis, pulmonary, acute general miliary	3	2.41	1.77	58.7	.51
Tuberculosis, general miliary.	2	1.61	1.18	45.6	.40
TOTAL FOR ENTIRE CLASS	169	135.85	100.00	131.3	100.00

the calendar year 1939. For 1939, with an average strength of 149,618, the admission rate was 1.00 per 1,000 with a non-effective ratio of 0.65 per 1,000. These figures indicate that definite progress is being made in the decline in the incidence of tuberculosis in the Navy. With the methods now in effect, and which are being instituted, this decline should continue.

The diagnosis of pulmonary tuberculosis in the Navy is the responsibility of the medical officer. He must be constantly on the watch for this condition. As already mentioned, the rather crowded living conditions aboard ship make the early diagnosis and isolation of all cases imperative. With the exception of destroyers, most of the larger units of the fleet are equipped with facilities for taking chest films. All have laboratory facilities for sputum examinations and blood counts. Once the diagnosis has been established, the transfer of the patient to the nearest Naval Hospital is made with the least possible delay. This is especially true in the tropics where delay in transfer to the States may result in rapid spread of the disease. Once the diagnosis has been made and the transfer to the nearest naval hospital accomplished the responsibility of the medical officer does not cease. Henceforth, he must be more alert than ever for the possible development of further cases. At the earliest opportunity he arranges for a chest survey on the entire ship's crew. This is usually done by means of roentgen photography using 35 mm. film. In addition, he has to arrange for a follow-up on the dependents of the case in question. Chest films and other diagnostic tests are arranged at the nearest outpatient department.

By no means least important is the role the medical officer plays in the education of the ship's personnel to the dangers of pulmonary tuberculosis. In talks to the ship's company he must discuss some of the more important symptoms and signs of this disease. He must also stress the importance of reporting to the sick bay immediately upon the development of symptoms referable to the respiratory tract.

The treatment of pulmonary tuberculosis in Navy personnel is confined almost entirely

TUBERCULOSIS (All Forms) 1937

DISEASE	Admissions	Admission rate per 100,000	% of class Admissions	Sick days per case	% of class sick days
Tuberculosis, pulmonary, chronic, active	123	92.58	80.92	145.5	86.00
Tuberculosis, unclassified.	18	13.55	11.84	129.3	9.56
Tuberculosis, pulmonary, chronic, arrested	5	3.76	3.29	75.4	2.19
Tuberculosis, pulmonary, acute, pneumonic	4	3.01	2.63	11.3	1.76
Tuberculosis, pulmonary, acute general miliary	2	1.41	1.32	93.5	.49
TOTAL FOR ENTIRE CLASS	152	114.41	100.00	139.8	100.00

TUBERCULOSIS (All Forms) 1938

DISEASE	Admissions	Admission rate per 100,000	% of class Admissions	Sick days per case	% of class sick days
Tuberculosis, pulmonary, chronic, active	108	77.58	89.26	151.4	88.02
Tuberculosis, unclassified.	5	3.59	4.13	121.0	5.47
Tuberculosis, pulmonary, chronic, arrested	4	2.87	3.31	102.6	4.64
Tuberculosis, pulmonary, acute, pneumonic	4	2.87	3.31	107.8	1.62
Tuberculosis, pulmonary, acute general miliary	0	0	0	38.0	.23
TOTAL FOR ENTIRE CLASS	121	86.92	100.00	144.3	100.00

to Naval Hospitals. The only exception to this rule is in the case of officers, midshipmen, nurses and enlisted men with long periods of service. These persons are transferred to the Army's Fitzsimmons General Hospital at Denver, Colorado, for treatment.

The period of hospitalization in naval hospitals is comparatively short; namely, six months. At the end of this period patients are transferred to the United States Veterans Administration for further treatment. Despite this relatively short period of treatment, collapse measures are instituted with the least possible delay. Treatment is carried out by medical officers who have received special training in the collapse therapy of pulmonary tuberculosis. Upon transfer of the patient to a Veterans Administration Facility, usually all that is required is continuation of the treatment already instituted in the Naval Hospital. Upon admission of all cases of pulmonary tuberculosis the local health departments are notified for the purpose of statistical record and for further check-up. Upon release or transfer of patients the local health department is also notified.

While a patient is under treatment in a Naval Hospital, as a public health measure open cases with positive sputum are not allowed liberty to go ashore where they might disseminate the disease.

The American Red Cross, through its social workers attached to Naval Hospitals, assists the patient in effecting his transfer to a Veterans Administration Facility usually near his home. It is the fixed policy of the Bureau of Medicine and Surgery, once a diagnosis of pulmonary tuberculosis has been established, to retire that individual permanently from the United States Naval Service regardless of the extent or degree of the lesion.

Through the medium of the Red Cross social workers who contact the family of the tuberculous patient, provision is made for the diagnosis of any further cases in the patient's immediate family. This work is usually carried out by the outpatient department. Should hospitalization of dependents be required, the Red Cross assists in finding low cost hospitalization and in some instances renders financial assistance. Following release from an institution these individuals may then receive pneumothorax refills and other treatment at the outpatient department. Here again close cooperation exists between the local health departments to which all cases are reported as a public health measure.

By far the greatest problem, however, lies in the elimination of endemic pulmonary tuberculosis among Naval personnel. Some of the methods for accomplishing this end have already been indicated. Already one important step has been made in this direction by the routine roentgen photography of all recruits entering the Naval Service. The following radiological findings are considered disqualifying:

1) Any evidence of reinfection (adult) type tuberculosis, active or inactive, exclusive of slight thickening of the apical pleura.

2) Evidence of active primary (childhood) type tuberculosis.

3) Inactive primary tuberculosis if the degree or extent of involvement appears to be of present or future clinical significance.

4) Evidence of fibrinous or serofibrinous pleuritis.

Another method of control not yet in general usage, but which will be used more and more in the future, lies in conducting chest surveys by means of roentgen photography in all Naval units ashore and afloat in which one or more cases of active pulmonary tuberculosis has been detected. In addition to these measures research is constantly being made on methods of improving ventilation and sanitation aboard ship. Air conditioning has, in some instances, been tried. The part of the medical officer in conducting this research and suggesting new methods of control is invaluable. The Bureau of Medicine and Surgery welcomes suggestions from all personnel along this line which contribute to this end. Accurate statistics and their analysis in the future will determine if the methods for the control of pulmonary tuberculosis in the Navy are yielding results.

U. S. Naval Hospital.

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Organization News

DR. CHEVALIER L. JACKSON GUEST SPEAKER FOR CUBAN CHAPTER

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Reading from left to right:

Senator Dr. Octavio Rivero, Governor; Dr. Antonio Navarrete, Regent; Dr. Chevalier L. Jackson, Guest Speaker; Dr. Luis Ortego, President; Dr. Gustave Aldereguia, President, Cuban Chapter.

—:—

Dr. Chevalier L. Jackson, Philadelphia, Pennsylvania, a Fellow of the American College of Chest Physicians, was the guest speaker at the meeting of the Cuban Chapter of the College which was held at the Medical School of the University of Havana, Tuesday, April 14. In addition to Dr. Jackson's talk, the following program was presented and all of the papers were delivered in Spanish supplemented by lantern slides and films.

Dr. Luis Ortega, *presiding*.

1) Introductory Speech, Dr. Gustave Aldereguia, President of the Cuban Chapter of the College.

2) X-Ray Study of the Internal Relief of the Respiratory Organs, Dr. Pedro L. Farinas, demonstrating a new mucosographic technic evolved by the author.

3) The Bronchoscope and Its Role in Modern Medicine, Dr. Chevalier L. Jackson.

4) Cases illustrating different aspects of tracheobronchial diseases, Drs. A. Antonetti, J. Gros, F. J. Menendez, P. Hernandez, J. G. Arrazuria, R. G. Mendoza, R. Meneses, A. Navarette.

5) Closing Remarks, Dr. Antonio Navarette, Regent of the American College of Chest Physicians.

OHIO CHAPTER HOLDS ANNUAL MEETING

The Ohio Chapter of the American College of Chest Physicians held its annual meeting at the Neil House, Columbus, Wednesday, April 29. This meeting was held in conjunction with the annual meeting of the Ohio State Medical Association. Dr. William F. Hulse, Cleveland, spoke on "The Otolaryngological Aspects of Tuberculosis."

The following officers were elected: Dr. David W. Heusinkveld, Cincinnati, President; Dr. Norbert S. Greene, Brecksville, Vice-President; Dr. Joseph B. Stocklen, Cleveland, Secretary-treasurer (re-elected). Dr. Louis Mark, Columbus, is the retiring President.

NEW JERSEY CHAPTER HOLDS ANNUAL MEETING

The New Jersey Chapter of the College held its annual meeting at Haddon Hall, Atlantic City, Wednesday, April 22. The meeting was held in conjunction with the annual meeting of the New Jersey State Medical Society. The meeting was called to order by Dr. Joseph R. Morrow, Ridgewood, President of the Chapter, and Dr. Paul K. Bornstein of Belmar was appointed Secretary *pro tem* in the absence of Dr. Charles I. Silk, Secretary-Treasurer of the Chapter.

Dr. Julian Johnston, Director, Department of Thoracic Surgery, University of Pennsylvania Hospital, Philadelphia, gave an inter-

esting talk on "Total Pneumonectomy," illustrated with pictures. A brief outline of his talk is presented:

A. Indications for total pneumonectomy
   1) Carcinoma
   2) Bronchiectasis
   3) Multiple Abscesses
   4) Tuberculosis
   5) Benign Adenoma, not cured by bronchoscopy
      (a) Carcinoma
          Diagnosis must be early
          Bronchoscopy
          Aspiration biopsy
          Exploratory incision
      (b) Bronchiectasis
          Pneumogram must be done with visualization of all five lobes.
      (c) Multiple Abscesses
          Refractive to drainage as an indication.
      (d) Tuberculosis
          Still in the stage of evolution

B. Preoperative Care
   1) Bronchoscopic drainage with aspiration is essential in bronchiectasis
   2) In his twenty case reports, he does not use a preoperative pneumothorax

C. Surgery
   1) Anesthesia
   2) CO_2 washed out so that patient took no voluntary respirations
   3) No rib resections are done
   4) Negative pressure pneumothorax instituted
   5) In any previous infected case, a thoracoplasty to obliterate the emphysema cavity
   6) To prevent postoperative pain, crushing of intercostal nerves two to seven

The discussion was opened by Dr. M. James Fine of Newark.

The Nominating Committee consisting of Drs. Samuel B. English, Glen Gardner, and Martin H. Collier of Grenloch, presented the following names for officers:

Dr. Joseph R. Morrow,* Ridgewood, President; Dr. Clyde M. Fish,* Pleasantville, Vice-President, and Dr. Paul K. Bornstein, Belmar, Secretary. These officers were unanimously elected.

An expression of thanks was given to Dr. Charles I. Silk, the retiring Secretary-Treasurer.

The Chapter voted to hold quarterly scientific sessions at various points throughout the state. The first of these sessions will be held at the Bergen Pines Sanatorium. It will be a luncheon meeting and a guest speaker will be invited. Members of the Chapter will also be invited to present papers of scientific interest.

The Reception Committee for the National Convention of the American College of Chest Physicians requested the cooperation of all the members of the Chapter and their presence at Atlantic City, June 6-8.

*Re-elected.

PENNSYLVANIA CHAPTER TO HOLD MEETING AT ATLANTIC CITY

The Pennsylvania Chapter of the College will hold a short business meeting following the dinner of the American College of Chest Physicians, Monday night, June 8, at the Dennis Hotel, Atlantic City. This meeting will be addressed by one of the officers of the College.

The President and Secretary of the Pennsylvania Chapter have asked all members of the Chapter to make plans immediately for accommodations in Atlantic City. Advance information suggests the possibility of a large attendance and in order to forestall any disappointments, this matter should be attended to immediately. The officers of the Pennsylvania Chapter will be looking forward to seeing you in Atlantic City.

NEW YORK CHAPTER MEETINGS

A symposium on diseases of the chest was arranged and sponsored by the New York State Chapter of the College and presented as a part of the scientific program of the New York State Medical Society meeting at the Waldorf-Astoria, New York City, April 30. This session was one of the best attended of the whole convention. Speakers were introduced by Dr. Martin Marino, the presiding chairman of the General Sessions. A resolution was introduced by Dr. Melson Strohm, President of the New York Chapter, to hold a similar symposium at the coming meeting of the State Medical Society in Buffalo. This resolution was unanimously passed by the delegates of the New York State Medical Society.

The annual election of officers for the New York State Chapter will be held at the Hotel Dennis, Atlantic City, on the evening of June 8, following the annual dinner and smoker of the College. It is hoped that every member of the New York State Chapter will attend the national meeting.

Book Reviews

THE AUTONOMIC NERVOUS SYSTEM: Anatomy, Physiology, and Surgical Treatment, by James C. White, M.D., Assistant Professor and Tutor in Surgery, Harvard Medical School, and Reginald H. Smithwick, M.D., Instructor in Surgery, Harvard Medical School. Second edition, 470 pages, 92 illustrations. Price $6.75. The Macmillan Company, New York, 1941.

This monograph which first appeared in 1935 has been extensively enlarged and revised. Those familiar with the first edition will find much new material in the second edition. The experience of many individuals during the past six years in the surgery of the sympathetic system has been digested and many procedures which were still in the experimental stage when the first book was written have been critically evaluated in the present edition.

An interesting chapter on the historical development of our knowledge of the visceral nervous system has been included. The anatomy, physiology, and pharmacology of the autonomic system are each given rather extensive treatment in separate chapters. These do not serve as an adequate review of all experimental work bearing on this subject. The material will probably be sufficient for the practitioner and surgeon and serves its purpose as an introduction to the clinical parts of the text. Considerable more attention has been given to the physiology and treatment of visceral pain than the title might indicate. A detailed discussion of methods of study in this field is included.

Part II of the book deals with the individual conditions in which ablations of the sympathetic system has been suggested. These include the effect on peripheral vascular disease, on bones and joints, and on a variety of conditions involving the head and neck, the heart and aorta, the lungs, the gastro-intestinal system, and the genito-urinary system are discussed in separate chapters. An excellent chapter on the treatment of hypertension by sympathetic surgery is included. Developments in this field which have been particularly rapid during the past six years are discussed in detail and extensive bibliography is included.

The short chapter on the lung discusses the early favorable reports of German, French, and Russian workers of sympathectomy on bronchial asthma. Recent work with larger postoperative periods of observation do not support this early enthusiasm. The authors state that "sympathectomy cannot be recommended for this condition." On the other hand total resection of the pulmonary vagal branches has more valid physiological backing. They believe that a wider clinical trial to this operation is indicated. They recommend "that as a preliminary to operation the effect on vital capacity of a deep bilateral paravertebral injection with procaine should be determined."

Part III is concerned with surgical technique. The illustrations, none of which are half-tones, are inferior to many available in the literature. This section will, however, serve as a starting point for further reading in this phase of the subject.

The book is a well organized and relatively complete monograph of this rapidly growing subject. There is much to commend it to the student of neurology, and the practitioner who is interested in the neurophysiological approach to problems of disordered visceral function and intractable pain. It will serve even the most advanced student and experimental worker as a source of much information and its many references of great help for further study.

Robert S. Dow.

THE BLOOD BANK AND THE TECHNIQUE AND THERAPEUTICS OF TRANSFUSIONS. By Robert A. Kilduffe and Michael DeBakey. Pp. 558, with 214 illustrations and one color plate. The C. V. Mosby Company, St. Louis, 1942.

As the names of the authors and the chapter headings listed below would suggest, this book covers the ground indicated by its title thoroughly and should be of value to anyone interested in the indications for blood transfusions, the technics of typing, matching, obtaining and storing blood or plasma, and in the methods of transportation and administration of blood or plasma transfusions.

The titles of the chapters in the order of appearance are History; Rationale, Indications, and Contraindications; The Military Aspects of Transfusion; Special Types of Transfusion; Technique of Blood Typing and Compatibility Tests; Anomalous Blood Typ-

ing Reactions: Their Nature, Causes, and Detection, and Methods for Their Elimination; The "Universal Donor" and the "Universal Recipient"; The Blood Bank; The Changes Which Occur in Stored Blood; The Biochemical Changes in Stored Blood; The Operation of a Blood Bank; Plasma Transfusion; The Preparation and Preservation of Citrated Plasma; The Preparation of Concentrated and Dried Plasma; Methods and Technique of Transfusion; Complications of Blood Transfusion.

At the end of each chapter is an extensive and well-chosen list of references. It does not discuss, as do some books on the same subject, the heredity of blood groups, the medicolegal aspects of blood groupings, or the anthropologic distribution of blood groups. A considerable number of different methods are described for each procedure, so that anyone using the book will find a choice from which he may select his method. It might be desirable, in subsequent editions, to have a critical discussion of the advantages and disadvantages of each procedure included to aid the physician in making his selection. Special attention is given to the military problems that may arise in the use of blood plasma and blood transfusions. The book is up to date, as is shown by the data on the Rh factor in blood transfusion reactions and erythroblastosis fetalis and of a description of the intramedullary transfusion technic. The style, on the whole, is clear, but the authors show a fondness for big words where simpler words would be equally effective: e.g., ineluctable, exegetically; and on page 67, the use of the French "dernier resort" instead of "last resort." There are a few errors which are unavoidable in a first edition and will doubtless be corrected in subsequent editions. Perhaps the most unfortunate of these is in the table on page 263, which is to illustrate the correct method of labeling of stored blood. After a discussion of the importance of the care and accuracy with which this should be done they record the blood group in the table as "B (II Moss)", when, of course, it should be "B (III Moss)".

On the whole, every laboratory doing much blood grouping, everyone responsible for the operation of a blood bank or of a plasma collection service, and every physician giving transfusions in civil or military practice will find the book of value.

Edwin E. Osgood, M.D.

THORACIC SURGERY by Charles W. Lester, A.B., M.D., F.A.C.S. Oxford Medical Outline Series, Oxford University Press, 1941. Price $2.00.

This is a very timely book of particular value to general surgeons, medical students and all physicians, as it presents, in outline form, the essentials of the anatomy and physiology of the thorax and its contents.

Anesthesia is discussed, as well as diseases of the chest wall, mediastinum, esophagus, pericardium, heart, pleura and lungs, with considerable space devoted to the surgical treatment of pulmonary tuberculosis.

The technique of oleothorax is not approved. I would suggest consulting an article on the same subject by the late Dr. Ray W. Matson, which appears in Goldberg's "Clinical Tuberculosis."

Tuberculous pleurisy is given as a contraindication for closed intrapleural pneumonolysis. If it is non-febrile, it is not a contraindication—neither is obliterative pleuritis, if contracting operable adhesions are responsible for premature lung expansion.

Another indication for the operation, not mentioned, is pressure phenomena, such as mediastinal displacement, downward pressure on liver or stomach (phrenic dyspepsia),—the result of high pressures necessary to maintain a satisfactory collapse of the lung in the presence of adhesions. The book is recommended.

R. C. M.

NEWS NOTE

A meeting will be held of the members of the College from the state of Maryland and the District of Columbia for the purpose of organizing a District Chapter of the College. This meeting has been scheduled for the Hotel Dennis, Atlantic City, New Jersey, Monday, June 8, at 9:00 P. M., in connection with the annual meeting of the College.

Dr. Wm. D. Tewksbury, Governor of the College for the District of Columbia, will preside and Dr. John H. Peck, Oakdale, Iowa, Past President of the College, will address the meeting. All members of the College from the state of Maryland and the District of Columbia are urged to attend this meeting which will follow the annual Smoker of the College.